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U S ARMY RESEARCH INSTITUTE
OF
ENVIRONMENTAL MEDICINE

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PROGRESS REPORT

RCS-MEDDH-288

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MEDICAL RESEARCH AND DEVELOPMENT COMMAND

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Project No. 6X98-01-001, Military Environmental Medicine

Task 01: Environmental Medicine

Subtask: Psychological Factors in Man's Response to Environment

Study 1. A systematic investigation of personality factors as variables related to human behavior under environmental stress

Investigator: B. J. Fine, Ph.D.

Description:

Experiments involving human subjects typically result in a large amount of unaccounted for inter- and intra-subject variability. This variability tends to lessen the accuracy of predictions relevant to the variables being investigated. Any means by which the source of this variability can be identified and controlled will improve the efficiency of predictions derived from experimental data. Personality characteristics of subjects have been shown to be related to many aspects of behavior and the lack of control of this variable may be one of the major sources of experimental-statistical error.

Personality research may also be viewed from the standpoint of developing a theoretical approach to the personality-environment relationship which may permit prediction of physiological, psychological, biochemical and other responses of individuals through a knowledge of their personality characteristics and characteristics of the environment to which they are exposed. The project is designed to determine the personality dimensions relevant to the prediction of human behavior under environmental stresses and to investigate the extent to which these variables or dimensions can predict such behavior. Studies designed to specifically test certain theoretically derived hypotheses will be carried out. In addition, personality measures will be obtained from studies designed with other major variables in mind in order to determine the role of personality in contributing to the results of these studies.

Progress:

Considerable time has been spent in studying current approaches to the study of personality to determine dimensions of personality which appear to be relevant to environmental variables. Previous work on theoretically and empirically derived dimensions of introversion-extraversion, neuroticism and psychotism will, for the time being, be the major personality dimensions used.

Data relevant to automobile driver accidents and violations were obtained from other investigators at the University of Minnesota in an effort to test certain predictions. Investigations have been, and are being,

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carried out to determine the role of personality variables in predicting human behavior under environmental stress conditions.

Summary and Conclusions:

A relationship between personality and motor vehicle accidents and violations has been established.

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Task 01: Environmental Medicine

Subtask: Studies of Indigenous Populations

Study 1. Human environmental relationships of thermal stress

Investigator: Jack M. Planalp, Ph.D.

Description:

This study consists of a field study in north central India, in a natural environment providing both cold stress and a high heat load, and among a population having widely divergent characteristics of nutrition, work regimen and sociocultural status. The primary objective is to determine how problems of heat and cold stress may be influenced and modified by variations in the human environment. A further objective is to provide a basis for comparison with and generalization to problems of thermal stress in military activities.

Progress:

Current activities involve the study of available sources and data relevant to the problem, and preparation for the initiation of field study proposed for November 1962.

Summary and Conclusions:

The research task is in its beginning stages.

Project 6X98-01-001, Military Environmental Medicine

Task 01: Environmental Medicine

Publications:

1. Fine, B. J. Introversion-extraversion and motor vehicle driver behavior. Submitted to Psychological Reports.
2. Kreider, M. B. Pathological effects of extreme cold on man. Chapter in Medical Climatology, Sidney Licht, Ed., 1962 (in press).

Project No. 6X98-01-001, Military Environmental Medicine

Task 02: The Biological Responses to Cold

Subtask: Temperature Regulation in the Cold

Study 1. The contribution of non-contracting muscle metabolism to non-shivering thermogenesis

Investigators: Thomas R. A. Davis, M.D., Fred R. Winsmann, M.S., Norman L. Cohen, B.S.*

Description:

Previous in vitro work using the Warburg technique has demonstrated that the uptake of oxygen in muscle slices of the acclimatized rat is greater than that of the unacclimatized rat. The present study was implemented to determine the ability of non-contracting in vivo muscle to produce heat in the cold.

Progress:

The technique of infusing arterial blood at a known flow into the hind leg of the lightly anaesthetized dog and measuring arterio-venous differences in oxygen content is used in this study. By this means, the oxygen consumption of the hind leg could be ascertained prior to cold exposure, during cold exposure, and after nerve-section of the sciatic nerve at the sciatic notch. To date, a group of seven acclimatized dogs has been investigated.

Summary and Conclusions:

During exposure to -10°C, acclimatized dogs increased metabolism of the perfused area two to three times. After nerve section metabolism did not show a statistical change. This finding indicates that the muscles of the hind limb of the acclimatized dog is able to produce thermogenesis in the absence of muscular contraction.

*C&OMD, QMR&E Command, Natick, Mass.

Project No. 6X98-01-001, Military Environmental Medicine

Task 02: The Biological Responses to Cold

Subtask: Acclimatization to Cold

Study 1. Mechanisms of human cold acclimatization

Investigator: Robert J. T. Joy, Major MC

Description:

Cold acclimatized man may be more resistant to cold injury - a fact demonstrated for laboratory animals. Human cold acclimatization has been demonstrated in this laboratory. The next stage in this research is a study of mechanisms of cold acclimatization in man, which will allow prophylactic and therapeutic intervention in the future. An investigation of possible cellular/biochemical changes in man is a basic first step toward understanding the mechanism of action of cold acclimatization. This study defines one such possible mechanism.

Progress:

Norepinephrine has been suggested as a mediator of non-shivering thermogenesis in the cold acclimatizing rat, with a decline in shivering accompanied by an increase in vasopressor and calorogenic responses to exogenous hormone. A search for parallel findings in man has shown a decline in shivering with maintenance of heat production. A study of further mechanisms of physiological cold acclimatization in man is reported here. Nine healthy males, ages 23-25, were infused with norepinephrine (0.15 ug/Kg/min) for 20 minutes before and after five 40 hour weeks of semi-nude exposure to 5°C. All infusions were performed in the basal state, in a quiet room at 80°F (subjects nude), after a 30-minute period of control measurements. Rectal temperatures and respiratory rates were unchanged either by the drug or the intervening cold exposure. The drug increased respiratory minute volumes and tidal volumes, and decreased heart rates, but equally so in both experiments. Mean skin temperatures were unaffected by the drug but were significantly ($p < .025$) higher after cold exposure (mean 1.9°F). The drug-induced increase above basal of systolic and diastolic blood pressures was significantly lower ($p < .025$) after cold exposure. Oxygen consumption was the same in both basal periods and was unaffected by the drug before cold exposure. After cold exposure, norepinephrine produced a significant ($p < .025$) increase in oxygen consumption (mean 18 cc/min/M²). These results show a changed sensitivity to norepinephrine in cold exposed man, with a decrease in vasopressor response and the development of a calorogenic effect of the drug. The data suggest that in man, as in the rat, norepinephrine may be a mediator of a non-shivering thermogenesis occurring with cold acclimatization.

Task 02 (Project No. 6X98-01-001) - Cont

Summary and Conclusions:

Man has a specific cellular response to the cold acclimatizing process, demonstrated by an increased responsiveness to a calorogenic agent - norepinephrine. This study demonstrates for the first time a true biochemical change in cold-acclimatized man, and makes possible future exploration of other mechanisms of action.

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Task 02: The Biological Responses to Cold

Subtask: Acclimatization to Cold

Study 2. Cold exposure and acclimation in alloxan diabetic rats

Investigator: Robert H. Poe, Capt., MC

Description:

Cold acclimatization involves certain metabolic alterations in both man and animal which are believed to result in an increased resistance to cold injury. The control of these alterations is to a large degree, endocrine, and insulin is one of the endocrines so incriminated. This study is an investigation as to the role of insulin in cold acclimatization in the rat.

Progress:

The alloxan diabetic rat offers the unique approach to the study of the role of insulin in cold acclimation in that we have an animal that has a deficiency of insulin and insulin alone. Twenty alloxan diabetic and twelve control rats were exposed to 4°C for forty-two days. It was found that the alloxan diabetic rats had a significantly greater mortality rate, incidence of cold injury, and tendency to shiver less before, during, and after cold acclimation than did their controls. Additional work is now underway to investigate the diabetic animal's ability to mobilize tissue glycogen in the cold.

Summary and Conclusions:

Insulin is indirectly related to the process of cold acclimatization and, in the rat at least, plays a role in resistance to cold injury. It was demonstrated for the first time that the alloxan diabetic animal reacts to cold in somewhat of a different manner than the normal and is more susceptible to cold injury.

Project No. 6X98-01-001, Military Environmental Medicine

Task 02: The Biological Responses to Cold

Subtask: Acclimatization to Cold

Study 3. The use of infra-red heat lamps as a test of cold acclimatization reaction

Investigator: Russell W. Newman, Ph.D.

Description:

This study is designed to establish a reliable technique capable of field application on large numbers of subjects which will reflect the state of cold acclimatization when compared to previous or future trials on the same subject.

Progress:

Three studies have been carried out and a fourth study initiated during FY-62:

1. Minimum heat requirements during cold acclimatization

a. Ten subjects who were undergoing a five-week cold acclimatization at 5°C (Study 1, this Subtask) were subjected to six weekly trials. Each subject was exposed to +35°F for 80 minutes dressed only in shorts and lying on a laced-web cot. The subject was surrounded by eight 250-watt infra-red heat lamps. The test consisted of the subject allowing himself to chill to the limit of his tolerance, followed by the briefest possible rewarming under the heat lamps. The cycle of cooling and rewarming continued for the duration of the 80 minute trial.

b. The average amount of heat required per trial decreased by approximately half for the 10-man group over the course of the cold acclimatization (significant at the 5% level). This could be interpreted as an increased tolerance to acute chilling or an increased ability to rearm under the superficial stimulus of the heat lamps or a combination of both. Although the results of this study were positive and reasonably reliable, the test placed an acute stress on the subject and required a very high level of subject motivation. It does not appear to be entirely satisfactory for the objective of this work.

2. Threshold of cold discomfort during cold acclimatization

a. The same ten subjects who took part in the Minimum Heat Requirements Study (paragraph 1 above) underwent weekly trials designed to pinpoint the sensory level between comfort and mild cold-discomfort using the same temperature condition and heat lamps as in 1 above. For this study the wattage output of the heat lamps was controlled by the subject through a motor-driven voltage-regulator, and the subject increased the wattage as he felt cold and decreased the wattage as soon as he felt warm over a 50-minute exposure.

b. No significant change occurred in the wattage requirements of the ten subjects over the course of cold acclimatization. This may have been due to technical difficulties in the test since it was almost impossible to meter the heat so that the extremities were in balance with the rest of the body. On the other hand, it is possible that the results would have been the same even without the extremity problem. The sensory perception of the level of mild cold discomfort may not change in a six-week period even though the acclimatized subject can tolerate far more cold stress than was possible prior to acclimatization.

3. Shivering level response to increasing cold stress

a. A variation of the tests reported in 1 and 2 above was used on 19 subjects at four dry-bulb temperatures: +40°F, +32°F, +24°F and +16°F. The subject wearing shorts and socks lay for 50 minutes on the cot used in previous studies and turned on eight 375-watt infra-red heat lamps for 10 seconds each time he felt a gross body shiver. The purpose of the heat lamps was to provide just sufficient heat to prevent the subject from going into a continuous gross shivering condition.

b. No reliability data were collected in this study since each subject underwent the test only once at each temperature condition. The average number of gross shivers per exposure increased significantly (1% level) with decreasing temperature as would be expected. The data are being analyzed for further information.

4. Seasonal cold acclimatization in a tactical airborne unit

A seasonal study of responses to a test similar to that used in paragraph 3 above was initiated in July 1962. Thirty-six subjects of the U.S. 82nd Airborne Division at Fort Bragg, N. C. were processed through a 50-minute exposure to +35°F in a portable climatic chamber. Thirty-one of these subjects were processed through the test twice in a three-week period and showed good reliability in the number of gross shivers recorded. Three subsequent tests on the same subjects are planned for the fall of 1962 and the winter and spring of 1963 to follow seasonal changes in the shivering response.

Summary and Conclusions:

The three studies reported in paragraphs 1, 2 and 3 above were designed to explore the feasibility and instrumentation requirements of the objective. The fourth study was successful in the collection of initial data for a longitudinal study of seasonal changes, but its ultimate success cannot be predicted at this time.

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Task 02: The Biological Responses to Cold

Subtask: Acclimatization to cold

Study 4. Cold acclimatization and cold tolerance in man

Investigators: T.R.A. Davis, M.D., R.J.T. Joy, Major, MC, T.E. Dee, M.S., W.L. Goddard, B.S., F.R. Winsmann, M.S.

Description:

Studies were carried out to determine if acclimatization to cold can be induced in man and whether or not this results in an increased tolerance to the effects of cold.

Progress:

Studies establishing the ability of man to acclimatize to cold as measured by the indices of body temperature, heat production and shivering, together with subjective indices of greater tolerance, have been completed.

The first phase of the tolerance study has just been completed. Ten subjects were acclimatized for five weeks to 5°C in shorts for a period of 8 hours daily. Prior to this period of acclimatization, the responses to a standard exposure of one hour to 5°C were measured. After acclimatization, the responses were measured during a one-hour exposure on separate occasions to temperatures of +5, 0, -5 and -10°C in order to determine the temperature at which the responses of body temperature, surface temperature, oxygen consumption, and shivering equate those obtained at 5°C prior to acclimatization. The difference between 5°C and the lower temperature will indicate the increase in tolerance achieved by acclimatization. Work on data is still in progress.

Summary and Conclusions:

The completed studies have demonstrated that man acclimatizes to cold by a decrease in shivering, a decrease in energy expenditure, a lowering of body temperature and an increase in non-shivering thermogenesis in the cold. These changes can be induced by cold exposure in the chamber or, of clothing is reduced, under natural conditions. The induced changes are not influenced per se by heat acclimatization and, if the cold acclimatization is maximal, it is retained over a period of at least one summer. The data completed so far on tolerance demonstrate that acclimatization increases tolerance by a 10°C shift in response to shivering and a 6°C shift in cold induced metabolism.

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Task 02: The Biological Responses to Cold

Subtask: Acclimatization to Cold

Study 5. Changes in body composition, cyclic vasodilatation and body heat storage in cold acclimatization

Investigators: R. F. Goldman, Ph.D. and G. Newcomb, M.A., in conjunction with a research project of Major R. J. T. Joy

Description:

The basic physiologic alterations that occur during the "cold acclimatization process" in man are still mostly based on conjecture drawn from animal studies. In conjunction with Study 1, this Subtask, preliminary investigations of several possible physiologic alterations were carried out.

Progress:

The following measurements were made on ten subjects during, before, and after cold acclimatization:

- a. Total body heat store and skin and core temperature relations;
- b. Percent body fat and subcutaneous and depot fat relations;

c. The "Lewis" response (hunting response) which is a cyclic vasodilatation of the digital vasculature during cold exposure of the hand. It is hoped that the results obtained might yield a better understanding of the process of acclimatization to cold. The data are being analyzed.

Summary and Conclusions:

Preliminary analysis suggests that total body heat storage and skin and core temperature relations (item a) are not altered detectably and that both items b and c deserve further investigation.

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Task 02: The Biological Responses to Cold

Subtask: Biology and pharmacology of responses to cold stress

Study 1. Cardiovascular response on the tilt-table to combined cold, starvation and inactivity

Investigators: M.B. Kreider, Ph.D. and J.A. Vaughan*

Description:

The ability of the cardiovascular system to maintain the blood pressure and pulse rate during orthostatic change is believed to reflect the fitness of the cardiovascular system. Thus, a greater rise of pulse rate and fall in blood pressure during titling means a deterioration in cardiovascular adjustment.

Both starvation and inactivity have been shown to produce a deterioration in this adjustment while the effect of cold exposure, alone or combined with starvation and inactivity, is unknown.

Progress:

The effect of complete starvation and inactivity was studied during a 2-week period of exposure, semi-nude, to 60°F with sedentary activity and complete caloric restriction. Six soldiers were measured a total of 13 times before, during and after the period of exposure. The Harvard Step Test was also performed before and after. The study has been completed and a rough draft of a report has been prepared.

Summary and Conclusions:

The difference in systolic pressure between the tilted and horizontal positions increased during the exposure period and then decreased to below the control level by the second day of recovery. These changes are believed to be due mainly to the cold because recovery from starvation and inactivity might be expected to require a longer time. Harvard Step Tests before and after the exposure period also confirm a maintained or increased fitness. Pulse rate differences between the tilted and horizontal position remained unchanged during the exposure period but increased slightly during recovery. This suggests a slight decrease of fitness.

It may be concluded that, even though an immediate decrease is taking place in the fitness of the cardiovascular system, the overall effect of this exposure is an increase in fitness which is probably due to the training effect of the constant cold on this system.

*CARI-FAA, Oklahoma City, Oklahoma

Project No. 6X98-01-001, Military Environmental Medicine

Task 02: The Biological Responses to Cold

Publications:

1. Joy, R. J. T. Response of normal men to infused norepinephrine before and after chronic cold exposure. Physiologist, 1962 (in press).
2. Poe, R. H. and T. R. A. Davis. Cold exposure and acclimation in alloxan diabetic rats. Am. J. Physiol., 1962 (in press).
3. Davis, T. R. A., D. R. Johnston and F. Bell. Seasonal acclimatization to cold in man. J. Appl. Physiol. 16:231, 1961.
4. Davis, T. R. A. The effect of cold acclimatization on the responses to acute exposure to cold. Temperature, its measurement and control in Science and Industry Symposium, 1961.
5. Davis, T. R. A. Chamber cold acclimatization in man. J. Appl. Physiol. 16:1011, 1961.
6. Joy, R. J. T., R. H. Poe, F. Berman and T. R. A. Davis. Some physiological responses to arctic living. Arch. Env. Health, Jan. 1962.
7. Davis, T. R. A. The effect of heat acclimatization on artificial and natural cold acclimatization in man. J. Appl. Physiol. Vol. 17, 1962 (in press).

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Task 03: The Biological Responses to Heat

Subtask: Temperature regulation in the heat

Study 1. Physiological responses to hot-wet environments

Investigators: P.F. Lampietro, Ph.D.*¹, E.B. Green, M.A., D.E. Bass, Ph.D. and R.F. Goldman, Ph.D.

Description:

This study was initiated to develop a simple means of predicting the tolerance limits over a wide range of hot environments using a body temperature of 102.5°F for a heart rate of 180 Beats/Min as the cutoff points during exposure. Previous experiments were performed in which nude men sat quietly over the range of environmental conditions: 80-130°FDB, 65-110°FWB, and a system for the prediction of "tolerance" of nude, sedentary men was developed from the data. A nomogram was prepared from the equation whose general form is: $TT = a (VP)^2 + b (VP)(DB) + c (DB)^2$ where TT = tolerance time, minutes VP = vapor pressure mm Hg, DB = dry bulb °F and a, b, and c are constants.

Progress:

Additional experiments were performed to determine the validity of this prediction system. The effect of prior acclimatization to work in the heat on the ability to tolerate hot-humid climates was briefly explored. It was found that tolerance to hot-wet environments can be reliably estimated using the prediction system mentioned above. Statistical analysis of the data are being performed to point out the limits of the system.

Summary and Conclusions:

Any combination of dry and wet bulb temperatures producing an ambient vapor pressure of 42 mm Hg or less can be endured for at least 3 hours. Prior acclimatization to work in the heat appears to be of little importance in its effect on tolerance under the conditions of these experiments. A series of graphs relating tolerance time to ambient vapor pressure, to Wet Bulb Globe Temperature (WBGT) and to ambient dry bulb temperature have been prepared. The best fit of the experimental data occurs when the relationship between tolerance time and WBGT is used.

*CARI-FAA, Oklahoma City, Oklahoma

Project No. 6X98-01-001, Military Environmental Medicine

Task 03: The Biological Responses to Heat

Subtask: The Biology and Pharmacology of Responses to Heat Stress

Study 1. The relation of blood flow to intestinal absorption.

Investigator: E. D. Jacobson, Major, MC*

Description:

It has been shown that intestinal absorption of fat and protein is affected by blood flow to the gut, i.e. reduced blood flow is associated with reduced or delayed absorption. Little is known about the effects of reduced blood flow to the gut on intestinal absorption of carbohydrates. The purpose of this study is to determine whether such reduced blood flow affects intestinal absorption of carbohydrates that are (a) passively absorbed and (b) actively absorbed.

Progress and Conclusions:

Experiments on dogs revealed that reduction of blood flow to the gut does not decrease absorption of carbohydrates until blood flow is entirely cut off.

Preliminary findings on healthy young soldiers indicate that exercise in the heat -- a condition associated with reduced gut blood flow -- does not significantly reduce intestinal absorption of sugars.

*WRAIR, Washington 12, D. C.

Project No. 6X98-01-001, Military Environmental Medicine

Task 03: The Biological Responses to Heat

Subtask: The Biology and Pharmacology of Responses to Heat Stress

Study 2. The effect of salicylate on men exercising in the heat

Investigators: E. D. Jacobson, Major, MC* and David E. Bass, Ph.D.

Description:

Salicylates are widely used febrifugic agents. Men exercising in the heat develop hyperthermia. Studies were undertaken to determine whether salicylates would reduce the hyperthermia of men walking in simulated desert or jungle conditions and whether salicylates would accelerate the acclimatization to heat that chronic exposure confers.

Progress and Conclusions:

1. High dose salicylate administration resulted in higher rectal temperatures and sweat losses than control or low dose regimens during acute exposure to exercise in the heat in either desert or jungle climates.
2. Acclimatization to exercise in the heat was impeded but not prevented by salicylate administration while the drug was given.

*WRAIR, Washington 12, D. C.

Project No. 6X98-01-001, Military Environmental Medicine

Task 03: The Biological Responses to Heat

Subtask: The Biology and Pharmacology of Responses to Heat Stress

Study 3. The body heat store of men working in the heat

Investigator: R. F. Goldman, Ph.D.

Description:

An apparent dichotomy exists between the medical status of a human with a rectal temperature of 102.5°F (39.1°C) at rest and the same individual working with a rectal temperature of 104°F (40°C). An analysis and comparison of the total body heat storage as calculated from skin and rectal temperature and as calculated from known increments of metabolic heat production in an environment where compensation for incremented heat production by additional sweat evaporation is impossible should help resolve this dichotomy. Additionally these data will be subjected to a dynamic analysis to determine the lags, time constants and mathematical transfer functions for the body heat storage resulting from a step metabolic heat input. The results of this analysis will be useful in setting up a computer simulator for the human temperature regulatory system.

Progress:

Ten subjects were exposed to an environment of 104°F d.b. 98°F w.b., an environment in which evaporative heat transfer is severely limited, but heat accumulation is slow enough just to allow safely for a three-hour exposure at rest (rectal temperature 102.5°F (39.1°C) at three hours at rest). Metabolic heat production was measured. Skin, rectal, ambient wet bulb, dry bulb and globe temperatures were continuously recorded. Total weight loss and water intake during exposure were tabulated. Observations were made during resting exposures and on three days on which a single fifteen minute treadmill walk at different energy expenditures (equivalent to total metabolic heat increments of 25, 50 and 75 KCal) interrupted the otherwise identical resting three hour exposure. An arbitrary exposure termination rectal temperature of 102.5°F (39.1°C) at rest was adopted, thus reducing exposure time. The computer is being programmed to perform most of the necessary calculations. A future study is being planned where periodic metabolic increments will be used so that the frequency domain analysis corresponding to the present time domain analysis will be available to check the model of the human thermal response derived from the present study.

Summary and Conclusions:

The increases in body heat storage seem well correlated with the

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amounts of extra heat produced by each of the three work levels. Thus, as it was hoped, the body was unable to dissipate the extra heat and it should be possible to relate the reduction in tolerance time to body heat storage, as well as to the measured rectal temperature.

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Task 03: The Biological Responses to Heat

Publications:

Lampietro, P. F., M. Mager and E. B. Green. Some physiological changes accompanying tetany induced by exposure to hot, wet conditions. J. Appl. Physiol. 16:409, 1961.

Project No. 6X98-01-001, Military Environmental Medicine

Task 04: Biology of Work

Subtask: Physical Conditioning

Study 1. Changes in specific gravity and body fat in overweight female adolescents as a result of weight reduction

Investigator: R. F. Goldman, Ph.D.

Description:

While data are available for the body composition of adults in terms of percent body fat standards, and some information is available with regard to changes in body composition with altered caloric intake, very little has been done to provide equivalent information for the adolescent. A cooperative investigation of these facets was therefore initiated on a group of obese adolescent girls attending a weight reduction summer camp.

Progress:

Underwater weighing and residual lung volume determinations were used to establish the specific gravity in 34 overweight female adolescents (Means: age 15 years, height 64 inches, weight 168 lbs) before and after seven weeks program of diet and exercise. The percent body fat determined from the specific gravity measurements will be correlated with other anthropometric measurements, but the study is completed in so far as the specific gravity determinations alone are concerned.

Summary and Conclusions:

Initially some 40 to 50% of the body weight of this population was fat. During the seven week program, average weight loss was 14 lbs., of which 90% was determined to be fat using the specific gravity measurements.

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Task 04: Biology of Work

Subtask: Work Performance and Fatigue in Military Tasks

Study 1. The energy cost of load carriage

Investigators: R. F. Goldman, Ph.D. and P. F. Iampietro, Ph.D.*

Description:

A compilation of energy requirements for military tasks was undertaken in response to the frequent need for this information in providing best estimate solutions to many military problems. Unavailable data was determined experimentally, particularly the relationship between grade and load and progression rate.

Progress:

Measurements of oxygen consumption were obtained on soldiers walking on treadmills at speeds of 1.5 to 4 miles per hour, grades of 3, 6 and 9 percent with loads of 10, 20 and 30 Kg. This study is now completed.

Summary and Conclusions:

Within the ranges studied, energy cost was proportional to the total weight displaced (i.e. energy cost/unit mass for a given speed and grade was a constant independent of the proportioning between subject weight and load). The data integrated well with available values for level walking in the literature and a graph was constructed for predictive use.

*CARI-FAA, Oklahoma City, Oklahoma

Project No. 6X98-01-001, Military Environmental Medicine

Task 04: Biology of Work

Subtask: Work Performance and Fatigue in Military Tasks

Study 2. Effect of reduced ration and method of load carriage on physical fitness and energy expenditure.

Investigators: M. B. Kreider, Ph.D., J. A. Vaughan,* T. E. Dee, M.S., H. Hanson and C. J. Grass

Description:

This study was designed to determine the effect of reduced ration and method of load carriage on physical fitness and energy expenditure of small groups of men operating on the Greenland icecap. The icecap was selected because it provided more realistic conditions than the laboratory environment and because this area provided somewhat unusual conditions which have not been investigated for their effect on man.

Progress:

To acquire this information twenty soldiers hiked ten miles a day on snowshoes during 2-10 day periods pulling a load on sleds or carrying it partly on their backs and partly on sleds on full or reduced (40 percent reduction below voluntary intake) rations. Fitness was measured by the Harvard Step Test and later compared with other indices of fitness. A new method of determining energy expenditure during walking based on the respiratory volume was utilized which was simple for field use and allowed measurements to be made over a long period of time. The study has been completed, the data analyzed and a rough draft of the report has been prepared.

Summary and Conclusions:

Reduction of caloric intake of 39 percent for ten days during a period of hard exercise did not alter the physical fitness as measured by the Harvard Step Test, but did increase the irritability and the feeling of fatigue. Energy expenditure calculated on body weight basis during sled pulling did not decrease on the reduced caloric intake. Weight was carried more efficiently on the sled than on the back during walking on the level surface of the icecap. Energy expenditure was higher in the afternoon than morning. It appeared that the monotony of living on the barren icecap aggravated morale problems.

*CARI-FAA, Oklahoma City, Oklahoma

Project No. 6X98-01-001, Military Environmental Medicine

Task 04: Biology of Work

Subtask: Effects of Climate on Task Performance

Study 1. Manual performance as a function of climatic variables

Investigator: R. E. Clark, Ph.D.

Description:

Variation in climatic variables is known to produce changes in human behavior capability. This program of work is aimed at the prediction and explanation of these changes. All ten known basic psychomotor responses are to be studied as functions of climatic variables. The objective is to gain predictive power for field performance of men when any psychomotor response, or combination of responses, is involved.

Progress:

Studies have been completed regarding three further factors that determine manual performance capability in the cold: practice level, the thermal conditions of training, and contralateral hand cooling.

Summary and Conclusions:

After approximately ten trials on a task which requires movement of the finger joints, practice level does not relate to changes in response decrement during cold exposure. The thermal conditions of training are highly relevant to later performance capability under any condition of exposure. For manual hindrance to be minimal, both warm and cold hand experience are required early in learning. Cooling of the contralateral hand while a warm hand is performing on a task led consistently to a facilitation of manual performance. However, when the performing hand was itself cold, contralateral hand temperatures were found to be irrelevant.

Project No. 6X98-01-001, Military Environmental Medicine

Task 04: Biology of Work

Publications:

1. Goldman, R. F. and P. F. Lampietro. The energy cost of load carriage. *J. Appl. Physiol.* 17:675, 1962.
2. Clark, R. E. and C. E. Jones. Manual performance during cold exposure as a function of practice level, and the thermal conditions of training. *J. Appl. Psychol.*, 1962 (in press).

Project No. 6X98-01-001, Military Environmental Medicine

Task 06: Biological Considerations in the Design of Engineered Environments

Subtask: Biological Limits and Requirements Affecting the Design of Conventional Clothing Systems

Study 1. Heat transfer between clothed man and environment.

Investigator: A. H. Woodcock, Ph.D.

Description:

Since clothing is the primary method used to protect man from extreme environmental conditions, it is essential that the fundamentals of this form of protection be clearly understood. During World War II the quantitative concept of the insulating value of clothing and the relation of heat loss to this insulation and the environmental temperature marked the beginning of a basic science of clothing. Since that time investigations, often of a theoretical nature, have been carried on to determine the basic capabilities and limitations of clothing in all environments. A new concept of a range of environmental conditions over which man can maintain thermal balance has been introduced. Since the upper limit of this range represents heat stress and the lower cold stress a generalized treatment of all environments can be used. Using this it can be shown that although increased clothing insulation has a basic advantage of reducing heat loss from the skin in cold environments, it also has a basic disadvantage of reducing the range over which thermal balance can be maintained. Treatment of clothing properties has been divided into two basic parts, the first dealing with equilibrium conditions and the second with non-equilibrium or dynamic conditions. Using the latter technique, the only existent interpretation of "damp penetrating cold" has been suggested.

Progress:

Previous work has been consolidated for publication in the open literature, with a thorough review of previous literature. A new technique for measuring transient heat flow through clothing has been devised and with it earlier theoretical predictions have been confirmed. Using these techniques the advantages and disadvantages of moisture absorbent textiles such as wool and non-absorbent materials such as the newer synthetics have been pointed out. Heat stress indices which have previously been based on nude man are being investigated and modified to include clothing parameters.

Summary and Conclusions:

A science of protective clothing is being evolved which can be applied to all environments. This will indicate the theoretical limitations of and capabilities of clothing as a protective device. In addition, it provides the basis for stress indices for clothed man.

Project No. 6X98-01-001, Military Environmental Medicine

Task 06: Biological Considerations in the Design of Engineered Environments

Subtask: Biological Limits and Requirements Affecting the Design of Specialized Systems which Influence the Soldier's Microenvironment

Study 1. Tolerance time for work in the heat when wearing CBR protective clothing ensembles

Investigators: R. F. Goldman, Ph.D. and G. Newcomb, M.A.

Description

Studies at Camp Pickett, Virginia in 1960 on CBR protective clothing had to be aborted when it became apparent that the degree of physiologic strain associated with wear of these ensembles (which have a restricted vapor permeability) in the heat was extreme. The objective of this program was a careful determination of the reduction of tolerance time for work in the heat produced by wearing the current CBR ensembles.

Progress:

Preliminary chamber studies were conducted and indicated that tolerance (T_r 102.5°F; pulse 180 bpm) for moderate work (300 Kcal/hr) would be reached in less than one hour for soldiers enclosed in current CBR protective clothing systems even at temperate ambient temperatures. A field study was carried out to delineate this reduction of the ability to work. Soldiers wore two different CBR ensembles both "open" for ventilation and "closed" for CBR protection while marching at 3.25 mph (50 min. march, 10 min. rest) at Ft. Lee, Virginia during August 1961. This study is now completed.

Summary and Conclusions:

At roughly 75°F ambient temperature or above, the inability to dissipate by sweat evaporation the metabolic heat produced by the working soldier dominated any effects of ambient temperatures (up to 92°F), resulting in tolerance times (102.5°F (34.1°C) rectal temperature) of approximately 30 minutes for a 3.25 mph march while wearing either CBR protective ensemble.

Project No. 6X98-01-001, Military Environmental Medicine

Task 06: Biological Considerations in the Design of Engineered Environments

Subtask: Biological Limits and Requirements Affecting the Design of Specialized Systems which Influence the Soldier's Micro-environment

Study 2. Evaluation of some intraclothing hot air distribution systems for rewarming man

Investigators: R. F. Goldman, Ph.D., in cooperation with C&OMD, QMR&E Command

Description:

Development work had been initiated on improving the usual heated shelter method of rewarming troops in cold environments by using intraclothing hot air distribution systems. Physiologic evaluation of several systems was undertaken in response to a request from C&OM Division, QMR&E Command.

Progress:

It was impossible to induce rewarming of the extremities in inactive soldiers at -40° in spite of a maximum heat input to the torso surface (enough to induce nausea; equivalent whole body insulation value 20° clo). It was even impossible to maintain extremity temperature by continuous application of such torso heating. However, heat provided directly to the extremities appears efficient for rewarming.

Summary and Conclusions:

The major requirement for auxiliary heating (if not the only requirement) is direct heat supply to the hands and feet.

Project No. 6X98-01-001, Military Environmental Medicine

Task 06: Biological Considerations in the Design of Engineered Environments

Subtask: Biological Limits and Requirements Affecting the Design of Specialized Systems which Influence the Soldier's Microenvironment

Study 3. Auxiliary heating for inactive soldiers in the cold

Investigator: R. F. Goldman, Ph.D.

Description:

The present required military characteristic for cold weather clothing specifies that the inactive soldier be provided 8 hours of tolerance at -40°F , 3 mph wind. Even with the best available Arctic clothing ensemble, within one or two hours, finger temperatures and within two or three hours toe temperatures drop to near danger levels when soldiers remain inactive at -40°F . In response to a request from C&MO Division, QMR&E Command, research was undertaken on the feasibility of providing auxiliary heating with minimum power.

Progress:

Using a knit glove and sock with integral electrical resistance wiring for heating, a series of six chamber studies was conducted: to relate power supplied to finger and toe temperature maintained; to select optimum maintenance temperature levels; to evaluate overshoot, lag and power conservation using a cyclic power system; to determine thermostat desirability, physical location and set points; and to develop within an 8 lb. limit a practical, portable power supply and auxiliary heating kit adequate to allow the required military characteristic to be met.

Summary and Conclusions:

A $6\frac{1}{2}$ lb. battery vest (120 w/hr capacity) and thermostated, knit-wired gloves and wired insulated boots is adequate for 6 hours of tolerance. Meeting the 8 hour requirement within an 8 lb. limit is now dependent on the state of the art in portable power supply. The physiologic requirements and design parameters are now known. Heating the extremities with 5 watts per hand and slightly less per foot is adequate to maintain finger and toe temperatures of approximately 60°F if heat is supplied continuously. If the heated handwear and footwear is thermostated, these power requirements must be doubled to overcome the lag of the system which allows the skin surface temperature to fall below 60°F . However, since the hands and feet are rewarmed to above 60°F by the rewarming overshoot which accompanies the

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thermostat lag, the actual total power consumption for the inactive individual is the same as when the continuous, unthermostated, heaters are used. Thus, thermostating does not conserve power if the subject remains inactive, but of course does during periods of activity, when auxiliary heating is unnecessary. Calculation has shown that this amount of heat input per se is not enough to produce the finger and toe temperatures observed under these ambient conditions. It appears that the supplied heat releases the vasoconstriction in the extremity which is in large part warmed by the increased circulation of the body heat. The resultant slight drop in core temperature is readily compensable by metabolic processes.

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Task 06: Biological Considerations in the Design of Engineered Environments

Subtask: Biological Limits and Requirements Affecting the Design of Specialized Systems which Influence the Soldier's Microenvironment

Study 4. Development of a thermalibrium suit

Investigators: R. F. Goldman, Ph.D. and G. Newcomb, M.A.

Description:

Present and envisioned future requirements for CBR protection require encapsulation of the soldier. A long term program, the "thermalibrium suit" project to develop an encapsulated clothing system with integrally powered suit environment conditioner has been undertaken by the Advanced Projects Office, C&OM Division, QMRA&EC. ARIEM is providing the necessary physiologic research to develop the engineering design parameter for such a system.

Progress:

An initial study was carried out using ventilation with ambient air (23 cfm) to cool subjects walking 3.25 mph in a research model encapsulated suit system under simulated temperate (70°F, 50% R.H.) tropic (85°F, 75% R.H.) and desert (110°F, 20% R.H.) environments. Sweat production, sweat evaporation, metabolic heat production and body heat storage were measured and balance (steady state) equations applied to estimate convective, radiative and evaporative exchange.

Summary and Conclusions:

Preliminary data analysis indicates that sweat production is adequate to provide the required cooling under all three environmental conditions. The efficiency of sweat evaporation (evaporation production) in the temperate condition is about 0.70, adequate for dissipation of metabolic heat and achievement of thermal balance. However, in the tropic and desert environments this efficiency is at present only about 0.42, with an efficiency of 0.55 apparently required. Design changes in the clothing system (e.g. improvement of wetted surface area for evaporative transfer, better distribution of the ventilating air and reducing present head gear weight) are being made. However, it is already obvious that the approach is feasible physiologically since sweat production has not yet reached maximum, and adequate enthalpy potential of the ventilating air is available. This is indicated by the fact that exhaust air is less than saturated under the test conditions described. Lower flow rates are also feasible since the exhaust air

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temperature is well below skin temperature for the tropic and temperate environments. This project will be a continuous one for several years. The information derived has of course general applicability to a wide range of problems (e.g. space suits).

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Project No. 6X98-01-001, Military Environmental Medicine

Task 06: Biological Considerations in the Design of Engineered Environments

Publications:

1. Woodcock, A. H. Moisture Permeability Index - a new index for describing evaporative heat transfer through fabric systems. QMR&E Command Tech. Rpt. EP-149, June 1961.
2. Goldman, R. F. Evaluation of some intraclothing hot air distribution systems for rewarming man. QMR&E Command Res. Study Rpt. Phy-2, July 1962.

Project No. 6X99-26-001, Basic Research in Life Sciences

Task 09: Physiology

Subtask: Functions of Tissues, Organs and Organ Systems

Study 1. The relation of blood flow to gastric secretion

Investigator: E. D. Jacobson, Major, MC*

Description:

To determine whether gastric secretion is a function of gastric blood flow.

Progress and Conclusions:

1. When gastric blood flow is increased, the rate of gastric secretion increases and the resistance to blood flow decreases.
2. When gastric blood flow is reduced, the rate of gastric secretion declines and the resistance to blood flow increases.
3. Drugs which stimulate the rate of gastric secretion, namely histamine, acetyl choline, gastrin and bradykinin, also decrease the resistance to blood flow in the stomach.
4. Norepinephrine, which inhibits gastric secretion, increases the resistance to blood flow in the stomach.

*WRAIR, Washington 12, D. C.

Project No. 6X99-26-001, Basic Research in Life Sciences

Task 09: Physiology

Subtask: Functions of Tissues, Organs and Organ Systems

Study 2. The evaluation of polyethylene glycol in the estimation of intestinal fluid volume

- Investigator: E. D. Jacobson, Major, MC*

Description:

The non-absorbable marker technique for estimating gut fluid volumes employing PEG has not been validated despite widespread use of this agent in human studies. An evaluation was undertaken.

Progress and Conclusions:

Close agreement was found in perfusion experiments between values for gut fluid volume estimated volumetrically and by the marker technique. Discrepancies, however, appeared when small volumes instilled in gut segments were estimated by the two methods. Analysis of the data indicates that the PEG estimates are more accurate than measurements made by removing fluid from the gut. The PEG technique appears validated for intact human and animal studies.

*WRAIR, Washington 12, D. C.

Project No. 6X99-26-001, Basic Research in Life Sciences

Task 09: Physiology

Subtask: Functions of Tissues, Organs and Organ Systems

Study 3. Changes in coagulation and fibrinolytic mechanisms as the result of exposure to heat, exercise and cold

Investigator: W. F. Blatt, Ph.D.

Description:

The coagulation and fibrinolytic mechanisms have been implicated in the reaction of animals and men to acute and chronic exposure to varying environmental stress situations. It is necessary to delineate these changes so that appropriate parenteral therapy may be instituted where necessary.

Progress:

Methods for the analysis of coagulant and fibrinolytic activity have been instituted. Samples from men subjected to environmental stress have been obtained and are under current investigation.

Conclusions:

None.

Project No. 6X99-26-001, Basic Research in Life Sciences

Task 09: Physiology

Subtask: Functions of Tissues, Organs and Organ Systems

Study 4. Humoral regulation of blood platelet levels

Investigators: W. F. Blatt, Ph.D. and D. P. Cooney, M.D.*

Description:

It has been suggested that control of blood platelet levels may be under humoral regulation. Isolation and characterization of the responsible agents is of importance in those conditions whereby altered platelet levels may be of clinical significance (thrombocytopenia and thrombocytosis).

Progress:

Two agents capable of influencing platelet levels have been extracted from bovine spleens. A report on the current status of this work has been delivered to the Office of The Surgeon General and a presentation of results has been given at a meeting at Oak Ridge, Tennessee on "Recent developments on studies of blood platelets."

Conclusions:

None.

*Stanford University Medical School, Palo Alto, California

Project No. 6X99-26-001, Basic Research in Life Sciences

Task 09: Physiology

Subtask: Functions of Tissues, Organs and Organ Systems

Study 5. Biochemical responses to environmental stress

Investigators: W. F. Blatt, Ph.D. and M. Mager, Ph.D.

Description:

Subtle biochemical responses underlie all physiological adaptations to acute and prolonged stress. The purpose of this subtask is to define the biochemical responses to heat and cold stress, and to relate them to associated physiologic adaptations.

Progress:

Workphase (1): Changes in circulating plasma free fatty acids (FFA) associated with cold exposure (Mager).

Since it has been demonstrated that circulating FFA increases with administration of epinephrine and norepinephrine, changes in plasma and urinary catecholamines may indicate the interrelationship of these substances in various stress conditions. In dogs and men exposed to prolonged periods of cold stress, plasma FFA levels were determined prior to, during, and following exposure. In another cold study, FFA determinations were made on men infused with norepinephrine prior to and immediately following a 5-weeks exposure period, and also during periods of induced shivering. Samples were also obtained for the determination of epinephrine and norepinephrine levels in plasma and urine throughout the entire course of the study.

Workphase (2): Stress induced changes in urinary protein composition (Mager and Blatt).

A complete biochemical examination of urinary proteins has been initiated in an attempt to characterize the changes induced by heat, exercise and cold stress. Urine samples were obtained following varied periods of exposure, and the soluble materials concentrated and assayed for: total solids, protein distribution, lipoprotein content, enzymatic activity, and immunologic identity with plasma components.

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Workphase (3): The effects of environmental stress on plasma protein composition (Blatt).

Serum protein composition is altered in a variety of pathologic conditions. These may reflect changes in nutritional status or changes in metabolic pathways. It appeared necessary to delineate the changes in protein and lipoprotein composition in men exposed to prolonged periods of heat and cold. Soldiers were subjected to varying degrees of environmental stress and serum samples obtained following varying periods of exposure. Electrophoretograms of protein and lipoprotein composition were obtained and the results will be compared with patterns obtained from normal non-stressed individuals.

Summary and Conclusions:

Final evaluation for all phases awaits completion of analysis.

Project No. 6X99-26-001, Basic Research in Life Sciences

Task 09: Physiology

Subtask: Functions of Tissues, Organs and Organ Systems

Study 6. The location of temperature regulating centers in the cat brain stem

Investigator: G. Clark, Ph.D.

Description:

To develop a better understanding of the central nervous processes of temperature regulation.

Progress:

Three cats with huge transverse lesions at the level of the optic chiasma have been prepared. They are now maintaining relatively normal temperatures at usual ambient temperatures and two are now eating spontaneously. Three cats with a hemisection at C_1 and a second contralateral hemisection at C_7 , midbrain and anterior hypothalamus, respectively, have been prepared. The one with the $C_1 - C_7$ hemisection proves to have about the same remaining abilities to regulate body temperature as a transection at C_7 . The other two have normal ability to withstand heat (as measured by panting level) while their body temperatures drop precipitously in the cold. Another C_1 hemisection and 2 with hemisections in the anterior midbrain, 2 between superior and inferior colliculi, and 2 at caudal border of midbrain have been prepared and are awaiting a second operation.

Summary and Conclusions:

There is no crossing of nerve fibers subserving either shivering or alterations in peripheral vasculature in the region between C_1 and C_7 . Furthermore, there is little or no crossing of such impulses between the anterior hypothalamus and C_1 . This indicates that there are probably no subsidiary centers in the lower brain stem for shivering and possibly none for the vascular responses to a cold stimulus.

Project No. 6X99-26-001, Basic Research in Life Sciences

Task 09: Physiology

Subtask: Functions of Tissues, Organs and Organ Systems

Study 7. The mechanism of myelin sheath staining

Investigators: G. Berube, B.S. and G. Clark, Ph.D.

Description:

This study is designed to realize more of the potential information afforded by myelin sheath stains.

Progress:

By means of various blocking procedures (histochemical) and controlled deamination it has been possible to show that a secondary amine is the essential grouping for myelin sheath stains of the Weil and Phosphotungstic Acid types; Luxol Fast Blue, PAS and Lendrum's Phloxine Tartrazine methods each utilize different functional groups, but do not stain secondary amines:

<u>Stain</u>	<u>Functional Group</u>
Weil	Secondary amine
PTAH	Secondary amine
Luxol	Acid OH (?)
Lendrum's Phloxine Tartrazine	??
PAS	Vicinal OH

Summary and Conclusions:

None.

Project No. 6X99-26-001, Basic Research in Life Sciences

Task 09: Physiology

Subtask: Functions of Tissues, Organs and Organ Systems

Study 8. The spinal localization of the shivering pathway in the spinal cord

Investigators: G. Clark, Ph.D. and E. B. Green, M.A.

Description:

There is no good information concerning the spinal pathway for shivering. This study was designed to develop a better understanding of the central nervous processes of temperature regulation.

Progress:

Six cats were prepared with differing partial lesions of spinal cord. All ultimately walked, but two were never able to void spontaneously. Despite the varying locations of the spinal cord lesion all exhibited the same effects on shivering when exposed to cold or given a moderate dose of nembutal. All of these cats could shiver, but the shivering below the lesions (as compared to areas with normal innervation) was sporadic, of low amplitude and required a very low skin temperature. These animals have been sacrificed and their spinal cords are now being prepared for study.

Summary and Conclusions:

Data to date would indicate either that the pathway is diffuse or that possibly two descending pathways are present, one possibly acting primarily on the gamma system while the other acts on anterior horn cells.

Project No. 6X99-26-001, Basic Research in Life Sciences

Task 09: Physiology

Subtask: Cellular Biology

Study 1. The lipids of human bovine platelets and their thrombo-plastic activity

Investigators: D. G. Therriault, Ph.D. and E. E. Woodside, Ph.D.*

Description:

It has been shown that lipid extracts of blood platelets will cause an acceleration of blood coagulation. Although there is general agreement that the coagulant effect of platelets is related in some way to their phospholipid content, opinion is by no means uniform as to the number of different compounds involved. The purpose of the present study was to separate and identify the phospholipid components of platelets and determine the clotting activity of each.

Progress:

By means of a column chromatographic technique, human and bovine platelets were found to contain free cholesterol, triglycerides, diglycerides, monoglycerides and phospholipids. Saturated and unsaturated hydrocarbons, esterified cholesterol and non-esterified fatty acids could not be detected. Of these, only the phospholipids exhibited clot promoting activity. A combination of countercurrent distribution and column chromatography was used to isolate and identify five major components of the phospholipid fraction: phosphatidylserine, phosphatidylethanolamine, lecithin, sphingomylin and inositol phosphatide. The five phospholipids isolated from platelets were tested in all possible combinations in a recalcification system, the thromboplastin generation test and a modified thrombin generation test. Only phosphatidylserine and phosphatidylethanolamine had clot promoting activity. The highest activity resulted from a combination of phosphatidylserine and lecithin.

Summary and Conclusions:

It was possible to determine the distribution of lipids in blood platelets by means of countercurrent distribution and column chromatography. As a result the phospholipids responsible for the clot promoting activity of platelets were identified.

*USARML, Fort Knox, Kentucky

Project No. 6X99-26-001, Basic Research in Life Sciences

Task 09: Physiology

Subtask: Cellular Biology

Study 2. Purification and identification of phosphatidylethanolamine

© Investigators: D. G. Therriault, Ph.D. and J. Kerkay, M.S.

Description:

Existing chromatographic methods for the separation of brain phospholipids proved inadequate for the purification of phosphatidylethanolamine. In this study a method was developed to obtain phosphatidylethanolamine from beef brain in a pure state.

Progress:

A crude lipid extract was first fractionated by countercurrent distribution in a solvent system consisting of carbon tetrachloride-methanol-water, 62:35:4 by volume. This resulted in the complete separation of phosphatidylserine from phosphatidylethanolamine. The phosphatidylethanolamine fraction was then purified by silicic acid column chromatography. The pure phosphatidylethanolamine was identified by paper chromatography of the intact phospholipid and of the acid hydrolysis products, as well as by elemental analysis.

Summary and Conclusions:

Chemically pure phosphatidylethanolamine was obtained by countercurrent distribution and silicic acid chromatography.

Project No. 6X99-26-001, Basic Research in Life Sciences

Task 09: Physiology

Subtask: Cellular Biology

Study 3. Column chromatographic separation of non-lipid contaminants from lipid extracts

Investigators: D. G. Therriault, Ph.D. and G. Rouser, Ph.D. *

Description:

Lipid extracts of biological material invariably contain non-lipid contaminants, the removal of which presents a difficult and often a time-consuming problem. The removal of non-lipids is essential in studies concerned with the quantitative determination of lipids in biological material.

Progress:

As much as 1.0 gm of lipid extract dissolved in chloroform-methanol 7:3 plus 3% water is applied to a cellulose column pretreated with methanol-water, 1:1 followed by equilibration with chloroform methanol 7:3 plus 3% water. The bulk of the lipid is eluted with 200 ml. of chloroform methanol 7:3 plus 3% water. By changing the eluting solvent to chloroform-methanol-water 4:15:1 by volume, gangliosides mixed with some non-lipid contaminants are eluted. The non-lipid material can then be eluted with methanol-water 1:1. Recovery of the applied material is 100%, and the gangliosides may be further purified by dialysis against distilled water. Chloroform-methanol extracts of beef brain contain approximately 10% non-lipid material.

Summary and Conclusion:

A column chromatographic technique was developed using cellulose powder packing to quantitatively separate non-lipid material from lipid extracts of beef brain.

*City of Hope Medical Ctr., Duarte, California

Task 09: Physiology

Subtask: Cellular Biology

Study 4. Effects of temperature and pH on the rate of oxygen dissociation from the red blood cell

Investigator: W. H. Lawson, Jr., Captain, MC

Description:

The equilibrium between oxygen and human red blood cells, oxyhemoglobin dissociation curve, has been studied by other investigators with respect to the effect of variable temperature and pH. Little work has been done on the effect of temperature and pH on the rate of deoxygenation of human red blood cells *in vitro*, i.e., the rate of approach to a new equilibrium at a lowered oxygen tension. With respect to oxygen exchange between blood and peripheral tissue, the equilibrium between blood and oxygen determines how much oxygen will be given up by the blood given time to reach equilibrium; and the rate of deoxygenation determines how rapidly this oxygen will be given up.

Progress and Conclusions:

1. Two different experimental lines of evidence indicate that $\text{Na}_2\text{S}_2\text{O}_4$ does not react with the hemoglobin inside intact red cells during the brief time of exposure.
2. Reducing blood temperature from 37°C to 7°C at pH 7.3 increases the half time for deoxygenation from 0.04 to 0.8 sec. There is a linear relationship between the log of the velocity constant, K_c (fraction of total change per second), and the reciprocal of the absolute temperature.
3. Decreasing pH from 7.3 to 6.7 at either 37° , 22° , or 5°C by increasing pCO_2 from 43 mm Hg (6%) to 149 mm (20%), decreases the half time by 30%. There is a linear relationship between K_c and pH.
4. Abrupt changes in pCO_2 and pH produced by reacting blood containing low CO_2 with an equal volume of reducing agent containing high CO_2 have only about 1/5 the effect of deoxygenation rate that would be expected from the pCO_2 and pH of the final mixture. This indicates that the time required for CO_2 to diffuse inside the red cell and form carbonic acid is limiting the effect of pH change in this situation.

5. Other investigators have shown that red cells remain in lung tissue capillaries for about 0.75 seconds in intact man at 37°C. At 7°C in vitro red cells have only given up about 1/2 of their oxygen in 0.75 seconds. Therefore, it would appear that red cells in peripheral cold tissues must spend more time in the capillaries else an oxygen debt occurs. Abrupt decreases in pH, as would occur when arterial blood at normal pH enters acidic tissue capillaries, only slightly reverses the decreased rate of deoxygenation produced by decreasing temperature.

Project No. 6X99-26-001, Basic Research in Life Sciences

Task 09: Physiology

Publications:

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